

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method for inhibiting the expression of a target transcript in vitro in mammalian cells comprising contacting the target transcript with a completely single-stranded RNA molecule having a length from 14-50 nucleotides wherein at least the 15 14 5' most nucleotides are completely complementary to said target transcript, and wherein said expression is inhibited by RNA-interference.

2. (Canceled)

3. (Previously presented) The method of claim 1 wherein said RNA molecule has a length from 15-29 nucleotides.

4. (Previously presented) The method of claim 1, wherein said RNA molecule has a free 5'hydroxyl moiety or a moiety selected from phosphate groups or analogues thereof.

5. (Previously presented) The method of claim 1, wherein said RNA molecule has 5'-moiety selected from the group consisting of 5'-monophosphate  $((\text{HO})_2(\text{O})\text{P}-\text{O}-5')$ , 5'-diphosphate  $((\text{HO})_2(\text{O})\text{P}-\text{O}-\text{P}(\text{HO})(\text{O})-\text{O}-5')$ , 5' triphosphate  $((\text{HO})_2(\text{O})\text{P}-\text{O}-(\text{HO})(\text{O})\text{P}-\text{O}-\text{P}(\text{HO})(\text{O})-\text{O}-5')$ , 5' guanosine cap (7-methylated or non-

methylated) (7m-G-O-5'-(HO)(O)P-O-(HO)(O)P-O-P(HO)(O)-O-5'), 5'-adenosine cap (Appp), and any modified or unmodified nucleotide cap structure (N-O-5'(HO)(O)P-O-(HO)(O)P-O-P(HO)(O)-O-5'), 5'-monothiophosphate (phosphorothioate; (HO)<sub>2</sub>(S)P-O-5'), 5'-monothiophosphate (phosphorothioate; (HO)(HS)(S)P-O-5'), 5'phosphorothiolate ((HO)<sub>2</sub>(O)P-S-5'); any additional combination of oxygen/sulfur replaced monophosphate, diphosphate and triphosphates, 5'-phosphoramidates, 5'alkylphosphonates (R=alkyl=methyl, ethyl, isopropyl, propyl,), and 5'alkyletherphosphonates.

6. (Previously presented) The method of claim 1, wherein said RNA molecule is completely complementary to said target transcript.

7. (Previously presented) The method of claim 1, wherein said RNA molecule comprises at least one modified nucleotide analogue.

8. (Previously presented) The method of claim 7, wherein the modified nucleotide analogues are selected from sugar-backbone- and nucleobase-modified ribonucleotides and combinations thereof.

9. (Canceled)

10. (Canceled)

11. (Previously presented) The method of claim 1, wherein said RNA molecule is formulated as a pharmaceutical composition which contains a pharmaceutically acceptable carrier.

12. (Previously presented) The method of claim 11, wherein said carrier is selected from cationic liposomes and cationic lipid formulations.

13. (Previously presented) The method of claim 1, wherein said RNA molecule is associated with biodegradable polymers or microparticles.

14. (Previously presented) The method of claim 13, wherein said RNA molecule is associated with biodegradable polymers or microparticles via a covalent coupling.

15. (Previously presented) The method of claim 14, wherein said covalent coupling occurs via the 3'-terminus of the RNA molecule.

16. (Previously presented) The method of claim 10 for diagnostic applications.

17-19. (Canceled)

20. (Currently Amended) A composition for inhibiting the expression of a target transcript by RNAi in vitro comprising an active agent a single-stranded RNA molecule having a length from 14-50 nucleotides, wherein at least the 15 14 5' most nucleotides are completely complementary to said target transcript.

21. (Canceled)

22. (Withdrawn) Purified human RISC having a molecular weight of from up to about 150-160 kDa.

23. (Withdrawn) The RISC of claim 22 comprising at least one member of the Argonaute family of proteins.

24. (Withdrawn) The RISC of claim 22 containing eIF2C1 and/or eIFC2 and optionally at least one eIFC3, eIFC4, HILI and HIWI.

25. (Withdrawn) The RISC of claim 22, further containing an RNA component.

26. (Withdrawn) A host cell or non-human host organism capable of overexpressing RISC.

27. (Withdrawn) A method of enhancing RNAi in a cell or an organism comprising causing said cell or organism to overexpress at least one component of RISC.

28. (Withdrawn) The method of claim 27 for screening applications.

29. (Withdrawn) The method of claim 27 for therapeutic applications.

30. (Withdrawn) An antisense siRNA precursor molecule in the form of a hairpin stem-loop structure comprising 19 to 29 base pairs in stem, wherein at least 14 nucleotides in the stem are substantially complementary to a target transcript.

31. (Withdrawn) The siRNA precursor molecule of claim 30 having a 3' overhanging end.

32. (Previously presented) The method of claim 5, wherein said oxygen/sulfur replaced triphosphate is 5'-alpha-thiotriphosphate or 5'-gamma-thiotriphosphate.

33. (Previously presented) The method of claim 5, wherein said 5'-phosphoramidate is  $(HO)_2(O)P-NH-5'$  or  $(HO)(NH_2)(O)P-O-5'$ .

34. (Previously presented) The method of claim 5, wherein said 5'alkylphosphonate is  $RP(OH)(O)-O-5'$  or  $(OH)_2(O)P-5'-CH_2-$ .

35. (Previously presented) The method of claim 5, wherein said 5'alkyletherphosphonate has an alkyl ether selected from the group consisting of methoxymethyl (MeOCH<sub>2</sub>-) and ethoxymethyl (RP(OH)(O)-O-5').

36. (Previously presented) The method according to claim 35, wherein said 5'alkyletherphosphonate is RP(OH)(O)-O-5', wherein R=alkylether.

37. (Canceled)

38. (Previously presented) The method of claim 1, wherein the single stranded RNA molecule is longer than 20 nucleotides and the 20 5' most nucleotides are substantially complementary to a target transcript.

39. (Previously presented) The method according to claim 1, wherein at least the 20 5' most nucleotides are completely complementary to said target transcript.

40. (Previously presented) The composition according to claim 20, wherein at least the 20 5' most nucleotides are completely complementary to said target transcript.

41. (Previously presented) The method according to claim 1, wherein said mammalian cells are human cells.

42. (Currently amended) A method for inhibiting the expression of a target transcript in vitro in mammalian cells comprising contacting the target transcript with a completely single-stranded RNA molecule having a length from 14-50 nucleotides wherein at least the 15 14 5' most nucleotides are completely complementary to said target transcript, and wherein said expression is inhibited by RNA-interference, wherein said RNA molecule has 5'-moiety selected from the group consisting of 5'-monophosphate ((HO)<sub>2</sub>(O)P-O-5'), 5'-diphosphate ((HO)<sub>2</sub>(O)P-O-P(HO)(O)-O-5'), 5' triphosphate ((HO)<sub>2</sub>(O)P-O-(HO)(O)P-O-P(HO)(O)-O-5'), 5' guanosine cap (7-methylated or non-methylated) (7m-G-O-5'-(HO)(O)P-O-(HO)(O)P-O-P(HO)(O)-O-5'), 5'-adenosine cap (Appp), and any modified or unmodified nucleotide cap structure (N-O-5'(HO)(O)P-O-(HO)(O)P-O-P(HO)(O)-O-5'), 5'-monothiophosphate (phosphorothioate; (HO)<sub>2</sub>(S)P-O-5'), 5'-monothiophosphate (phosphorothioate; (HO)(HS)(S)P-O-5'), 5' phosphorothiolate ((HO)<sub>2</sub>(O)P-S-5'); any additional combination of oxygen/sulfur replaced monophosphate, diphosphate and triphosphates, 5'-phosphoramidates, 5'alkylphosphonates (R=alkyl=methyl, ethyl, isopropyl, propyl,), and 5'alkyletherphosphonates.

43. (New) A method for inhibiting the expression of a target transcript in vitro in mammalian cells comprising contacting the target transcript with a single-stranded RNA molecule having a length from 15-29 nucleotides wherein said single-stranded RNA molecule is completely complementary to said target transcript, and wherein said expression is inhibited by RNA-interference.

44. (New) A method for inhibiting the expression of a target transcript in vitro in mammalian cells comprising contacting the target transcript with a completely single-stranded RNA molecule having a length from 15-29 nucleotides wherein at least the 15 5' most nucleotides are completely complementary to said target transcript, and wherein said expression is inhibited by RNA-interference.